

Smooth Muscle Precursor Cells Derived from Human Pluripotent Stem Cells for Treatment of Stress Urinary Incontinence.

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Public Summary:

There is great interest in using stem cells (SC) to regenerate deficient urethral muscles in patients with urinary incontinence. There is loss of smooth muscle cells in the urethral muscles with aging, surgery, or birth trauma. This eventually will present as urinary incontinence. Current efforts for urethral muscle restoration rely on adult mesenchymal stem cells as cell source. These adult stem cells obtained from muscle biopsies do not yield sufficient smooth muscle cells (SMC) for transplantation. We may be able to overcome this limitation by using pluripotent SC (PSC) to derive SMCs. Hence, we sought to investigate whether smooth muscle precursor cells (pSMCs) derived from human PSCs can restore urethral function in an animal model of urinary incontinence generated by surgical urethral injury. Rats were divided into four groups: control (no intervention), sham saline (surgery+saline injection), bladder SMC (surgery+human bladder SMC injection) and treatment (surgery+pSMC injection, which includes human embryonic stem cell (hESC) Hg-derived pSMC and induced pluripotent stem cell (iPSC)-derived pSMC). pSMCs (2×10^6 cells/rat) were injected into the urethra 3 weeks after surgery. Urethral muscle pressure was measured 5 weeks post injection. iPSC-derived-pSMC treatment groups showed significantly higher pressures compared to the saline-treated rats, consistent with restoration of urethral muscle function. Our data indicate that pSMCs derived from human PSCs (hESC and iPSC) can restore urethral function.

Scientific Abstract:

There is great interest in using stem cells (SC) to regenerate a deficient urethral sphincter in patients with urinary incontinence. The smooth muscle component of the sphincter is a significant contributor to sphincter function. However, current translational efforts for sphincter muscle restoration focus only on skeletal muscle regeneration because they rely on adult mesenchymal SC as cell source. These adult SC do not yield sufficient smooth muscle cells (SMCs) for transplantation. We may be able to overcome this limitation by using pluripotent stem cell (PSC) to derive SMCs. Hence, we sought to investigate whether smooth muscle precursor cells (pSMCs) derived from human PSCs can restore urethral function in an animal model generated by surgical urethrolisis and ovariectomy. Rats were divided into four groups: control (no intervention), sham saline (surgery + saline injection), bladder SMC (surgery + human bladder SMC injection), and treatment (surgery + pSMC injection, which includes human embryonic stem cell (hESC) Hg-derived pSMC, episomal reprogrammed induced pluripotent stem cells (iPSCs)-derived pSMC, or viral reprogrammed iPSC-derived pSMC). pSMCs (2×10^6 cells/rat) were injected periurethrally 3 weeks postsurgery. Leak point pressure (LPP) and baseline external urethral sphincter electromyography were measured 5 weeks postinjection. Both iPSC-derived pSMC treatment groups showed significantly higher LPP compared to the sham saline group, consistent with restoration of urethral sphincter function. While the difference between the Hg-derived pSMC treatment and sham saline group was not significant, it did show a trend toward restoration of the LPP to the level of intact controls. Our data indicate that pSMCs derived from human PSCs (hESC and iPSC) can restore sphincter function.

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